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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/424,940	03/07/00	CRESS M	212662-1

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LOUIS C. CULLMAN
OPPENHEIMER WOLFF & DONNELLY
840 NEPORT CENTER DRIVE
SUITE 700
NEWPORT BEACH CA 92660

EXAMINER	
NICKOL,G	
ART UNIT	**PAPER NUMBER**
1642	9

DATE MAILED: 06/19/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/424,940	CRESS ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with th corr spondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-21* is/are pending in the application.

4a) Of the above claim(s) *6,7 and 11-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5 and 8-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☒ Other: *notice to comply* .

DETAILED ACTION

The response filed on April 30, 2001 (Paper No. 7) to the restriction requirement of March 28, 2001 has been received. Applicant has elected Group I, claims 1-5, and 8-10 for examination. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP 818.03(a). Claims 6-7, and 11-21 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Thus, claims 1-5, and 8-10 are pending and are currently under examination.

Specification

The specification is objected to for improper disclosure of amino acid sequences without a respective sequence identifier (SEQ ID NO:); for example, see page 12. Hence, the disclosure fails to comply with the requirements of 37 CFR 1.821 through 1.825. In the absence of a sequence identifier for each sequence, Applicant must provide a computer readable form (CRF) copy of the sequence listing, an initial or substitute paper copy of the sequence listing, as well as any amendment directing its entry into the specification, and a statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 CFR 1.821(e-f) or 1.825(b) or 1.825(d).

The specification is further objected to for the following reason: The specification on page 1 should be amended to reflect the priority status of the present application. For example:

This application claims benefit to provisional application 60/048405, filed June 3, 1997, now abandoned.

Information Disclosure Statement

The IDS submitted (Paper No. 5) has been considered, in part. Citation No. CD (Schwarz et al.) was not written in English, therefore only the abstract of this reference could be considered. Further, the IDS was modified to include Class/Subclass headings for US Patent Documents.

Claim Rejections - 35 USC § 112

Claims 3-4 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 3-4 are indefinite for reciting amino acids "15-21" as there is no frame of reference to determine which specific amino acids are being claimed. This rejection can be obviated by amending the claims to include a specific sequence identifier (SEQ ID NO:) for amino acids 15-21.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 8-9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for detecting cancer in a subject comprising contacting a blood sample obtained from the subject with an antibody that binds an epitope on a blood protein degradation peptide, does not reasonably provide enablement for the method as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *Ex parte* Forman, 230 USPQ 546 (BPAI 1986). They include the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are broadly drawn to a method for detecting cancer in a subject comprising contacting a biological sample obtained from the subject with an antibody that binds an epitope on a blood protein degradation peptide that is masked in the blood protein and determining the presence of an antibody-peptide complex.

This includes detecting cancer in a subject *in any and all types of biological samples* including but not limited to urine, cervical secretions, bronchial aspirates, sputum, saliva, feces, serum, synovial and cerebrospinal fluid.

The specification teaches (page 11, lines 16) that the present invention is directed at a method for measuring the quantity of proteolytic degradation products of "serum" proteins. The specification further teaches (page 17-19) that serum samples from cancer patients generally exhibited higher concentrations of FDP, using the D_m/F format, than did control patients, and that scatterplots derived from serum samples of control patients and cancerous patients demonstrated increased sensitivity of FDP measurements relative to measurements of other cancer antigens (page 21).

One cannot extrapolate the teachings of the specification to the scope of the claims because the claims are broadly drawn to detecting cancer in all types of biological samples, and applicant has not enabled detection in all of these types of samples because it has not been shown that these blood protein degradation products are capable of being detected in anything but blood samples. Hence, to one of ordinary skill in the art, it would not be predictable nor could one reasonably expect that such blood protein degradation products are detected in all types of biological samples and that such detection would be indicative of cancer versus normal biological samples.

The specification provides insufficient guidance with regard to these issues and provides no working examples which would provide guidance to one skilled in the art that blood degradation products are detected in all types of biological samples. Reasonable correlation must exist between the scope of the claims and scope of enablement set forth, and it cannot be predicted from the disclosure that the claimed method would be enabled for detecting the blood proteins in all types of biological samples. Therefore, undue experimentation would be required to enable the claims as written.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5,8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Koopman et al. (J.Lab.Clin.Med., Vol. 109, No. 1, 1987, page 75-84).

The claims are drawn to a method for detecting cancer in a subject comprising contacting a biological sample obtained from the subject with an antibody that binds an epitope on a blood protein degradation peptide that is masked in the blood protein and determining the presence of an antibody-peptide complex (Claim 1); wherein the blood protein is fibrinogen (Claim 2); wherein the antibody recognizes an epitope comprising the amino acids 15-21 of the β-chain of human fibrinogen (Claim 3); wherein the antibody is monoclonal (Claim 4); wherein the presence of the antibody-peptide complex is determined by an assay comprising an enzyme-linked immunoadsorbent assay (Claim 5); wherein the subject is a mammal (Claim 8); wherein the subject is a human (Claim 9); wherein the biological sample is a blood sample (Claim 10).

Koopman et al. teach a method for detecting cancer (page 81, 2nd column) in a human comprising contacting a blood sample with a monoclonal antibody using an assay comprising an enzyme-linked immunoadsorbent assay wherein the antibody binds an epitope on a blood protein degradation peptide (FDP) that is masked in the blood protein wherein the blood protein is fibrinogen (abstract). In addition to correlating FDP with ovarian cancer, Koopman et al. further

teach that FDP is also observed in various kinds of untreated tumors and that the FDP assay might provide relevant information in addition to that provided by tumor markers such as CA-125. (bottom of page 82, top of page 83). Although the reference(s) do not specifically teach that the antibody recognizes an epitope comprising the amino acids 15-21 of the β-chain of human fibrinogen, the claimed antibody appears to be the same as the prior art , absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claims 1-5,8-10 are further rejected under 35 U.S.C. 102(b) as being anticipated by McCulloch et al. (Haemostasis, Vol. 20, pages 73-80, 1990) as evidenced by Koopman et al. (J.Lab.Clin.Med., Vol. 109, No. 1, 1987, page 75-84).

The claims are set forth above.

McCulloch et al. teach a method for detecting cancer in a human comprising contacting a blood sample with a monoclonal antibody using an assay comprising an enzyme-linked immunoadsorbent assay (page 73, under *Laboratory Methods*). Further, as evidenced by Koopman et al., the antibody binds an epitope on a blood protein degradation peptide (FDP) that is masked in the blood protein wherein the blood protein is fibrinogen. Although the reference(s)

do not specifically teach that the antibody recognizes an epitope comprising the amino acids 15-21 of the β-chain of human fibrinogen, the claimed antibody appears to be the same as the prior art , absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed product is different from those taught by the prior art and to establish patentable diffrences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later

invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amiral et al. (Blood Coag. Fibrinol., Vol. I, No. 4-5, pages 447-452, 1990, IDS) in view of Okajima et al. (Thrombosis Res. Vol. 66, pages 717-727, 1992, IDS) and Schwarz et al. (ACTA Medica. Sustriaca, Vol. 8, No.1, 1981, abstract only, IDS)

The claims are set forth above.

1. Amiral et al. teach a sensitive ELISA method for detecting blood degradation peptides in a human comprising contacting a blood sample (human blood- bottom of page 448) with a monoclonal antibody(s) wherein the antibody binds an epitope on a blood protein degradation peptide that is masked in the blood protein wherein the blood protein is fibrinogen (abstract, introduction, and page 449, Figure 1). Amiral et al. further teach that assays specific for the degradation products provide useful tools for accurate diagnosis in all pathologies where an imbalance in the coagulolytic equilibrium is generated (page 450, 2nd column, last sentence).
2. Amiral et al. do not specifically teach detection of cancer except to suggest that the assays provide complementary information in clinical states such as leukaemias and other disorders(abstract).
3. Schwarz et al. teach that fibrinogen degradation products could be detected frequently in patients with metastasized tumor disease.

4. Okajima et al. teach direct evidence for systemic fibrinogenolysis in a patient with metastatic prostate cancer which suggests that degradation products of fibrinogen would increase in the blood of cancer patients (abstract, and page 725).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to modulate the method of Amiral et al. so as to include the detection of cancer since it was well known in the art that fibrinogenolysis and fibrinogen degradation peptides were diagnostic of cancer. One would have been motivated to do so because Amiral et al. teach a sensitive assay for the detection of fibrinogen degradation products in plasma and suggest that "primary fibrinogenolysis may be present and, in this case, only fibrinogen degradation peptides are formed (FgDP). This concerns some malignancies such as prostate or meningioma. " (page 447). Hence, one of skill in the art at the time the invention was made would have a reasonable expectation of success for detecting cancer in a subject comprising contacting a biological sample obtained from the subject with an antibody that binds an epitope on a blood protein degradation peptide that is masked in the blood protein and determining the presence of an antibody-peptide complex. Further, although the reference(s) do not specifically teach that the antibody recognizes an epitope comprising the amino acids 15-21 of the β-chain of human fibrinogen, the claimed antibody appears to be the same as the prior art , absent a showing of unobvious differences. The office does not have the facilities and resources to provide the factual evidence needed in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is on the applicant to prove that the claimed

product is different from those taught by the prior art and to establish patentable differences. See In re Best 562F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray 10 USPQ 2d 1922 (PTO Bd. Pat. App. & Int. 1989).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
June 15, 2001

SUSAN UNGAR, PH.D
PRIMARY EXAMINER